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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/993,289	11/23/2001	George Jackowski	2132.092	5383

21917 7590 10/21/2003

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EXAMINER	
CHEU, CHANGHWA J	

ART UNIT	PAPER NUMBER
1641	12

DATE MAILED: 10/21/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/993,289	JACKOWSKI ET AL.	
	Examiner	Art Unit	
	Jacob Cheu	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 July 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 39-46* is/are pending in the application.

4a) Of the above claim(s) *39-43* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 9 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Applicant's amendment filed on July 15, 2003 has been received and entered into record and considered.

The following information provided in the amendment affects the instant application:

1. Claims 2-38 are cancelled.
2. Claims 39-46 are added to the instant application.
3. Applicant submits a declaration under 37 CFR § 1.132 has bee received.
4. Currently, claims 1, 39-46 are pending for examination.

Restriction/Election

1. The newly submitted claims 39-43 direct to an invention that is independent or distinct from the invention originally claimed because the claimed peptides in claim 1 can be materially practiced by a different method other than the added claims 39-43, such as separation or isolation process. Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 39-43 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

2. Applicant requests to rejoin the newly added method claims 39-46 to the amended claim 1 for examination on the ground that if the recited peptides in claim are novel, then the subsequently claims regarding on methods and kits limited to its use should be entitled to be rejoined with the novel product claims for examination. Applicant's arguments have been considered but appear not convincing, *in part*, because (b) the recited peptides in claim 1 are not novel and anticipated by Bernard et al. (see below 35 U.S.C §102(b) rejection), and the recited kit claims 44-46 are unpatentable over Bernard et al. in view of Hutchens et al.. (See below 35 U.S.C §103(a) rejection) Therefore, claims 39-43 are not entitled for rejoining with claim 1 for examination.

3. Therefore, currently claims 1 and 44-46 are under examination.

Enablement

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1, 44-46 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

As set forth in *In re Wands, 858 F .2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988)*, enablement requires that the specification teach those skilled in the art to make and use the invention without undue experimentation. Factors to be considered in determining, whether a disclosure would require undue experimentation include 1) the nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the quantity of experimentation necessary, 7) the relative skill of those in the art, and 8) the breadth of the claims.

The invention is directed to diagnostic markers for Alzheimers disease (AD) by obtaining a sample from a patient, subjecting the sample to mass spectrophotometric analysis, isolating and identifying a biopolymer marker that correlates to a biopolymer marker having a sequence identified such as SEQ ID NO. 1- 4. However, the specification lacks support to show that the instant recited biomarkers positively correlates with the AD disease. Although applicants assert that Figure 1, "a photograph of a gel which is indicative *of the* presence/absence of the marker in disease vs. control, ... " (page 46,

second paragraph) and the different bands, i.e. proteins now called as different SEQ ID in the instant application, "were found to be *predicative of AD disease.*" (supra, first paragraph) Nevertheless, it is not clear to one ordinary skill in the art as to how to use the recited invention for a positive diagnosis of AD disease. One of the fatal defects is that the reliability of the experimental results as described in Figures 1 and 2. In another word, applicant fail to specify the sample size, i.e. how many patients and healthy people participate in the study. In general, sample size is a prerequisite for rendering statistical correlation between any biomarker and the attributed disease. Since applicant does not provide any information as to the size of the patients and control healthy people conducted in the experiments, it inevitably imposes potential statistical shortcomings, namely false positive, false negative and ultimately no reliability at all.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claim 1 rejected under 35 U.S.C. 102(b) as being anticipated by Bernard et al. (Biochemistry (1985) 24: 2698-2704), is maintained.

5. Bernard et al. teach isolation and characterization of human cellular fibronectin encompassing the current recited peptides SEQ ID No. 1 and 4. (See Figure 3) Therefore, the reference of Bernard et al. reads on and anticipates the instant claim 1. It is noted that the recitation of diagnostic on Alzheimers disease has not been given patentable weight because the recitation occurs in the preamble. A preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. See *In re Hirao*, 535 F.2d 67, 190

USPQ 15 (CCPA 1976) and *Kropa v. Robie*, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951).

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

8. Claims 44-46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bernard et al. in view of Hutchens et al. (USP 6225047).

9. Bernard et al. reference has been discussed but is silent in teaching having peptides and the antibodies capable of binding to the peptides in a kit for conventional convenience, economy and reproducibility. Nevertheless, the Board of Patent Appeals and interferences has taken the position that once an antigen has been isolated, the manufacture of monoclonals antibodies against it is *prima facie* obviuos. See Ex parte Ehrlich, 3 USPQ 2d 1011 (PTO Bd. Pat. APP. & Int. 1987), Ex parte Sugimoto, 14 USPQ 2d 1312 (PTO Bd. Pat. APp. & Int. 1990).

Furthermore, Hutchens et al. teach immobolizing specific antibodies on the substrate in detecting ligand of interests. (See figure 14; Abstract) Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have provided Beranard with the kit containing antibodies immobilized on substrates as taught by Hutechens et al., for conventional convenience, economy and reproducibility in immunological detection of analytes. It is noted that the recitation of diagnostic on Alzheimers disease has not been given patentable weight because the recitation occurs in the preamble. See *In re Hirao*, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and *Kropa v. Robie*, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951).

Response to Applicant's Arguments

Enablement Rejections - 35 USC § 112, first paragraph

10. Applicant submits a §1.132 declaration described the SEQ ID No 1-4 peptides in AD patients compared to the control ones. Applicant also directs examiner's attention to the details on Figures 1 and 2 for the discovery of the recited peptides in AD patients. Applicant's argument has been considered but is not persuasive. As discussed before, applicant fails to provide the sample size for the necessary statistical analysis, i.e. patient number versus healthy control ones. It is important to reveal such information for establishing the reliability of the recited "diagnostic biomarkers" for the disease of interest. The current claimed invention lacks the statistical representation in a general population for a generic well-known disease. Assuming *arguendo*, there is a definite sample size as shown by Figure 1 (patient labels- AD-H-S-004, AD-H-S-005, AD-H-S-006, AD-H-S-008 versus AG- AD-H-S-002 to AG-AD-H-S-005), the sample size (total 9) is too small to be considered statistically reliable. Therefore, simply gathering data from Figure 1 and 2, with a limited sample size, cannot serve molecular diagnostic purpose in a general population.

Rejection – 35 U.S.C 102 (b)

11. Applicant argues that the Bernard et al. reference does not specifically teach the recited peptides (SEQ ID No. 1-4), and no where does Bernard et al. teach the specific peptides serve as a diagnostic marker for AD disease. Applicant's argument has been considered but is not persuasive. First, the instant claim 1 directs to peptide products claim. Accordingly, the intended use is not given any patentable weight consideration. See *In re Hirao*, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and *Kropa v. Robie*, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951). Second, although Bernard et al do not specifically teach the recited peptides per se, the teachings of Bernard et al. still encompass and read on the instant claim 1. Because applicant does not refrain the instant recited peptides in a limited segment. The wording "a biopolymer marker peptide" can be interpreted as broadly as to be anticipated by Bernard et al. reference.

Conclusion

12. No claim is allowed.

13. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jacob Cheu whose telephone number is 703-306-4086. The examiner can normally be reached on 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 703-305-3399. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-305-3399.

Jacob Cheu
Examiner
Art Unit 1641

October 6, 2003

LONG V. LE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600
10/20/03